## **Amendment to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

1. (Currently amended) An Actinium-225 complex comprising a functionalized polyazamacrocyclic chelant compound of the formula I, hereinbelow:

$$G \xrightarrow{Q} N \xrightarrow{T} Q$$

wherein:

$$\nearrow$$

T is

$$L \xrightarrow{\begin{pmatrix} X \\ C \\ Y \end{pmatrix}_m} (CH_2)_n - C - (CH_2)_r - C$$

G is independently hydrogen or

each Q is independently hydrogen, (CHR<sup>5</sup>)<sub>p</sub>CO<sub>2</sub>R or (CHR<sup>5</sup>)<sub>p</sub>PO<sub>3</sub>R<sup>6</sup>R<sup>7</sup> or

$$L \xrightarrow{\begin{pmatrix} X \\ | \\ C \\ | \\ Y \end{pmatrix}_m} (CH_2)_n \xrightarrow{Q^1} (CH_2)_r \xrightarrow{\qquad}$$

 $Q^1$  is hydrogen,  $(CHR^5)_wCO_2R$  or  $(CHR^5)_wPO_3R^6R^7$ ; each R is independently hydrogen, benzyl or  $C_1$ - $C_4$  alkyl;  $R^6$  and  $R^7$  are independently H,  $C_1$ - $C_6$  alkyl or  $(C_1$ - $C_2$  alkyl)phenyl; each R<sup>5</sup> is independently hydrogen; C<sub>1</sub>-C<sub>4</sub> alkyl or

(C<sub>1</sub>-C<sub>2</sub> alkyl)phenyl;

with the proviso that at least two of the sum of Q and Q<sup>1</sup> must be other than hydrogen;

A is CH, N, C-Br, C-Cl, C-SO<sub>3</sub>H, C-OR<sup>8</sup>, C-OR<sup>9</sup>N<sup>+</sup>-R<sup>10</sup>X<sup>-</sup>, or

$$C = C \longrightarrow R^{11}$$

Z and Z<sup>1</sup> independently are CH, N, C-SO<sub>3</sub>H, N\*-R<sup>10</sup>X-, C-CH<sub>2</sub>-OR<sup>8</sup> or C-C(O)-R<sup>11</sup>;

 $R^8$  is H,  $C_1$ - $C_5$  alkyl, benzyl, or benzyl substituted with at least one  $R^{12}$ ;  $R^9$  is  $C_1$ - $C_{16}$  alkylamino;

R<sup>10</sup> is C<sub>1</sub>-C<sub>16</sub> alkyl, benzyl, or benzyl substituted with at least one R<sup>12</sup>; R<sup>11</sup> is O (C<sub>1</sub>-C<sub>2</sub> alkyl), OH or NHR<sup>13</sup>;

R<sup>12</sup>-is H, NO<sub>2</sub>, NH<sub>2</sub>, isothiocyanato, semicarbazido, thiosemicarbazido, maleimido, bromoacetamido or carboxyl;

 $\mathbb{R}^{13}$ -is- $\mathbb{C}_1$ - $\mathbb{C}_5$ -alkyl;

X and Y are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-carbon bond;

n is 0 or 1;

m is an integer from 0 to 10 inclusive;

p is 1 or 2;

r is 0 or 1;

w is 0 or 1;

with the proviso that n is only 1 when X and/or Y form an additional carbon-carbon bond, and the sum of r and w is 0 or 1;

L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula Appln. No. 10/664,670 Response October 13, 2004 Reply to Office Action of August 6, 2004

$$R^1$$
  $Cyc$   $CH_2)_t$ 

wherein:

s is an integer of 0 or 1;

t is an integer of 0 to 20 inclusive;

R<sup>1</sup> is H, NO<sub>2</sub>, NH<sub>2</sub>, isothiocyanato, semicarbazido, thiosemicarbazido, maleimido, bromoacetamido or carboxylor an electrophilic or nucleophilic moiety which allows for covalent attachment to a biological carrier, or synthetic linker which can be attached to a biological carrier, or precursor thereof; and

Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to a biological carrier selected from the group consisting of a protein, antibody, antibody fragment, hormone, peptide, growth factor, antigen or hapten;

with the proviso that when R<sup>1</sup> is H, the linkage to the biological carrier is through one of Q or Q<sup>1</sup>; and with the proviso that when R<sup>1</sup> is other than H, at least one of Q and Q<sup>1</sup> must be (CHR<sup>5</sup>)<sub>p</sub>PO<sub>3</sub>R<sup>6</sup>R<sup>7</sup>; and with further proviso that when Q is (CHR<sup>5</sup>)<sub>p</sub>CO<sub>2</sub>R, Q<sup>1</sup> is (CHR<sup>5</sup>)<sub>w</sub>CO<sub>2</sub>R, R is H, R<sup>5</sup> is H, and R<sup>1</sup> is H, then the sum of m, n, p, r, s, t, and w is greater than 1;

or pharmaceutically acceptable salt thereof; complexed with <sup>225</sup>Ac.

- 2. (Original) A conjugate comprising the complex of Claim 1 covalently attached to a biological carrier.
- 3. (Original) The conjugate according to Claim 2 wherein the biological carrier is a protein, antibody, antibody fragment, hormone, peptide, growth factor, antigen or hapten.
- 4. (Cancelled)

 (Currently amended) The complex according to Claim 1 wherein the functionalized chelant is a compound of formula II

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wherein:

each Q is independently hydrogen, (CHR<sup>5</sup>)<sub>p</sub>CO<sub>2</sub>R or (CHR<sup>5</sup>)<sub>p</sub>PO<sub>3</sub>R<sup>6</sup>R<sup>7</sup> or

$$L \xrightarrow{\begin{pmatrix} X \\ - \\ C \\ Y \end{pmatrix}_m} (CH_2)_n - C \xrightarrow{\downarrow} (CH_2)_r - \cdots$$

 $Q^1$  is hydrogen,  $(CHR^5)_wCO_2R$  or  $(CHR^5)_wPO_3R^6R^7$ ; each R is independently hydrogen, benzyl or  $C_1$ - $C_4$  alkyl;  $R^6$  and  $R^7$  are independently H,  $C_1$ - $C_6$  alkyl or  $(C_1$ - $C_2$  alkyl)phenyl;

each  $R^5$  is independently hydrogen;  $C_1\text{-}C_4$  alkyl or

(C<sub>1</sub>-C<sub>2</sub> alkyl)phenyl;

with the proviso that at least two of the sum of Q and Q<sup>1</sup> must be other than hydrogen;

X and Y are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-carbon bond;

n is 0 or 1;

m is an integer from 0 to 10 inclusive;

p is 1 or 2;

r is O or 1;

w is O or 1;

with the proviso that n is only 1 when X and/or Y form an additional carbon-carbon bond, and the sum of r and w is 0 or 1;

L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula

$$R^1$$
 (Cyc)<sub>s</sub> (CH<sub>2</sub>)<sub>t</sub>

wherein:

s is an integer of 0 or 1;

t is an integer of 0 to 20 inclusive;

R<sup>1</sup> is H-, NO<sub>2</sub>, NH<sub>2</sub>, isothiocyanato, semicarbazido, thiosemicarbazido, maleimido, bromoacetamido or carboxylor an electrophilic or nucleophilic moiety which allows for covalent attachment to a biological carrier, or synthetic linker which can be attached to a biological carrier, or precursor thereof; and

Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to a biological carrier selected from the group consisting of a protein, antibody, antibody fragment, hormone, peptide, growth factor, antigen or hapten;

with the proviso that when R<sup>1</sup> is H, the linkage to the biological carrier is through one of Q or Q<sup>1</sup>; and with the proviso that when R<sup>1</sup> is other than H, at least one of Q and Q<sup>1</sup> must be (CHR<sup>5</sup>)<sub>p</sub>PO<sub>3</sub>R<sup>6</sup>R<sup>7</sup>; and with further proviso that when Q is (CHR<sup>5</sup>)<sub>p</sub>CO<sub>2</sub>R, Q<sup>1</sup> is (CHR<sup>5</sup>)<sub>w</sub>CO<sub>2</sub>R, R is H, R<sup>5</sup> is H, and R<sup>1</sup> is H, then the sum of m, n, p, r, s, t, and w is greater than 1;

or pharmaceutically acceptable salt thereof.

6. (Currently amended) The complex according to Claim 1 wherein the functionalized chelant is a compound of formula III

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wherein:

each Q is independently hydrogen, (CHR<sup>5</sup>)<sub>p</sub>CO<sub>2</sub>R or (CHR<sup>5</sup>)<sub>p</sub>PO<sub>3</sub>R<sup>6</sup>R<sup>7</sup> or

$$L \xrightarrow{\begin{pmatrix} X \\ C \\ Y \end{pmatrix}_m} (CH_2)_n \xrightarrow{Q}^1 (CH_2)_r - C$$

Q<sup>1</sup> is hydrogen, (CHR<sup>5</sup>)<sub>w</sub>CO<sub>2</sub>R or (CHR<sup>5</sup>)<sub>w</sub>PO<sub>3</sub>R<sup>6</sup>R<sup>7</sup>;

each R is independently hydrogen, benzyl or  $C_1$ - $C_4$  alkyl;  $R^6$  and  $R^7$  are independently H,  $C_1$ - $C_6$  alkyl or  $(C_1$ - $C_2$  alkyl)phenyl;

each  $R^5$  is independently hydrogen;  $C_1\text{-}C_4$  alkyl or

(C<sub>1</sub>-C<sub>2</sub> alkyl)phenyl;

with the proviso that at least two of the sum of Q and Q<sup>1</sup> must be other than hydrogen;

X and Y are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-carbon bond;

n is 0 or 1;

m is an integer from 0 to 10 inclusive;

p is l or 2;

r is O or 1;

w is O or 1;

with the proviso that n is only 1 when X and/or Y form an additional carbon-carbon bond, and the sum of r and w is 0 or 1;

L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula

$$R^1$$
 (Cyc)<sub>s</sub> (CH<sub>2</sub>)<sub>t</sub>

wherein:

s is an integer of 0 or 1;

t is an integer of 0 to 20 inclusive;

R<sup>1</sup> is H-, NO<sub>2</sub>, NH<sub>2</sub>, isothiocyanato, semicarbazido, thiosemicarbazido, maleimido, bromoacetamido or carboxylor an electrophilic or nucleophilic moiety which allows for covalent attachment to a biological carrier, or synthetic linker which can be attached to a biological carrier, or precursor thereof; and

Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to a biological carrier selected from the group consisting of a protein, antibody, antibody fragment, hormone, peptide, growth factor, antigen or hapten;

with the proviso that when R<sup>1</sup> is H, the linkage to the biological carrier is through one of Q or Q<sup>1</sup>; and with the proviso that when R<sup>1</sup> is other than H, at least one of Q and Q<sup>1</sup> must be (CHR<sup>5</sup>)<sub>p</sub>PO<sub>3</sub>R<sup>6</sup>R<sup>7</sup>; and with further proviso that when Q is (CHR<sup>5</sup>)<sub>p</sub>CO<sub>2</sub>R, Q<sup>1</sup> is (CHR<sup>5</sup>)<sub>w</sub>CO<sub>2</sub>R, R is H, R<sup>5</sup> is H, and R<sup>1</sup> is H, then the sum of m, n, p, r, s, t, and w is greater than 1;

or a pharmaceutically acceptable salt thereof.

- 7. (Original) A conjugate according to Claim 2 comprising the <sup>225</sup>Ac complex of DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) covalently attached via amide linkage to a biological carrier.
- 8. (Original) A conjugate according to Claim 2 comprising the <sup>225</sup>Ac complex of 2-(p-isothiocyanatobenzyl)-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid covalently attached to a biological carrier.
- 9. (Original) A pharmaceutical formulation comprising the <sup>225</sup>Ac conjugate of Claim 2 and a pharmaceutically acceptable carrier.
- 10. (Original) The formulation of Claim 9 wherein the pharmaceutically acceptable carrier is a liquid.
- 11. (Original) A method of therapeutic treatment of a mammal having cancer which comprises administering to said mammal a therapeutically effective amount of the formulation of Claim 9.